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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/955,373	10/21/1997	SOREN MOURITSEN	BNIT0003-US	7254

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EXAMINER	
SCHWADRON, RONALD B	

ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
02/17/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

david.hoffman@bn-it.com

Office Action Summary	Application No.	Applicant(s)	
	08/955,373	MOURITSEN ET AL.	
	Examiner	Art Unit	
	Ron Schwadron, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *88-100 and 102-112* is/are pending in the application.

4a) Of the above claim(s) *88-100,104 and 106-110,112* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *102,103,105 and 111* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/24/10 has been entered.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. The rejection of claims 102,103,105,111 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons elaborated in the previous Office Action is withdrawn in view of the amended claims.

4. Claims 102,103,105,111 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is no support for the new limitation recited in claim 102. Regarding applicants comments about the specification, page 3, lines 28-30, said passage states:

The epitopes substitute the self-protein fragments, thus preserving the overall secondary and tertiary structure of the self-protein to a large extent.

Thus, said passage discloses that the secondary and tertiary structure are preserved to a large extent. The claim only recites that the secondary and tertiary structure is essentially preserved and thus differs in scope from the disclosure in the specification.

The disclosure provided in the specification is not commensurate in scope with the claimed invention (aka the claimed invention constitutes new matter).

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. The rejection of claims 102,103,105,111 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the reasons elaborated in the previous Office Action is withdrawn in view of the amended claims.

7. Claims 102,103,105,111 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 102 is indefinite in the recitation of "the secondary structure and tertiary structure of the self-protein is essentially preserved" because it is unclear what this means or encompasses. It is unclear what changes to the secondary and tertiary structure would or would not be encompassed by the aforementioned term. For example, it is unclear if this term encompasses changes at the physical/chemical level (eg. crystal structure) or simply functional changes (eg. still immunogenic antigen as evidenced by antibody binding by antibodies specific for unmodified antigen). If the term is interpreted as encompassing changes at the physical/chemical level, it is unclear as to what deviations from the normal crystal structure would or would not be encompassed by the term "the secondary structure and tertiary structure of the pathogenic self-protein is essentially preserved". It is unclear as to what changes to the secondary structure would or would not be encompassed by the aforementioned term. For example, it is unclear if this term encompasses changes at the physical/chemical level (eg. crystal structured) or simply functional changes (eg. still immunogenic antigen as evidenced by antibody binding by antibodies specific for unmodified antigen). If the term is interpreted as encompassing changes at the physical/chemical level, it is unclear as to what deviations from the normal crystal structure would or would not be encompassed by the term "essentially preserve the overall secondary structure".

Regarding applicants comments, the fact that the analog induces an antibody response does not define what changes to the secondary and tertiary structure would or would not be encompassed by the aforementioned term. For example, it is unclear if this term encompasses changes at the physical/chemical level (eg. crystal

structure) or simply functional changes (eg. still immunogenic antigen as evidenced by antibody binding by antibodies specific for unmodified antigen). If the term is interpreted as encompassing changes at the physical/chemical level, it is unclear as to what deviations from the normal crystal structure would or would not be encompassed by the term "the secondary structure and tertiary structure of the pathogenic self-protein is essentially preserved". It is unclear as to what changes to the secondary structure would or would not be encompassed by the aforementioned term. For example, it is unclear if this term encompasses changes at the physical/chemical level (eg. crystal structured) or simply functional changes (eg. still immunogenic antigen as evidenced by antibody binding by antibodies specific for unmodified antigen). If the term is interpreted as encompassing changes at the physical/chemical level, it is unclear as to what deviations from the normal crystal structure would or would not be encompassed by the term "essentially preserve the overall secondary structure".
The limitation under consideration is only recited in cited passage of the specification, page 3, wherein there is no definition of said term. Regarding the Delcayre declaration, it is noted that Delcayre is an employee of the assignee of the instant application.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 102 is rejected under 35 U.S.C. 103(a) as being unpatentable over Russell-Jones et al. (WO 92/05192) in view of Dean et al. (US Patent 5,716,596) and Bona et al. (US Patent 5,969,109).

Russell-Jones et al. teach T cell epitopes derived from Trat protein (see Abstract). Russell-Jones et al. teach Trat T cell epitopes are inserted into proteins, wherein the insertion of said peptide increases the antibody response against the protein into which Trat has been inserted (see page 4, lines 24-26 and Abstract). Russell-Jones et al. teach that the Trat peptide is inserted such that the protein still functions as an immunogen. The Trat peptide has been inserted into the immunogen in such a manner as to essentially preserve the overall secondary structure, because the ability of the immunogen to function as an immunogen is maintained (see page 8, first complete paragraph). Whilst the term "secondary structure of the pathogenic self-protein is essentially preserved" is indefinite as per above, for the purposes of this rejection it will be assumed the aforementioned limitation encompasses the ability of the immunogen to function as an immunogen is maintained. Russell-Jones et al. teach that the Trat modified immunogen can be used as a vaccine in a composition containing an adjuvant such as saponin (see page 8 and 13). Russell-Jones et al. teach that using recombinant DNA technology that Trat peptide can be inserted into the immunogen via substituting Trat peptide for a peptide contained in said molecule (see page 32 and page 31, first incomplete paragraph). In addition, Bona et al. also teach that a T cell epitope can be substituted into a particular region of a target molecule wherein the T cell epitope retains immunogenicity (see column 11, second paragraph and column 4). Russell-Jones et al. teach that immunogens used in the aforementioned vaccines can include self proteins such as luteinizing hormone, somatostatin, inhibin, FSH (see page 9 and claim 12). Russell-Jones et al. teach that such vaccines can be used in animals and humans. Somatostatin is a "self protein" in view of its art recognized role in a variety of diseases (see Dean et al., column 2, first paragraph and column 6, third paragraph from bottom). Russell-Jones et al. do not teach use of the particular immunodominant foreign T cell epitopes recited in the claim. Russell-Jones et al. teach that immunodominant foreign T cell epitopes derived from diphtheria toxoid were known in the art (see page 4, first paragraph). Russell-Jones et al. teach that diphtheria toxoid has already been approved for use as a carrier for human vaccines (see page 14, fist paragraph). It would have been prima facie obvious to one of ordinary skill in the art at

the time the invention was made to have created the claimed invention because Russell-Jones et al. teach the claimed method except for use of immunodominant foreign T cell epitopes derived from diphtheria toxoid, Bona et al. also teach that a T cell epitope can be substituted into a particular region of a target molecule wherein the T cell epitope retains immunogenicity, Russell-Jones et al. teach that immunodominant foreign T cell epitopes derived from diphtheria toxoid were known in the art and that diphtheria toxoid was already approved as a carrier for human vaccines. One of ordinary skill in the art would have been motivated to do so because immunodominant foreign T cell epitopes derived from diphtheria toxoid were known in the art and diphtheria toxoid was already approved as a carrier for human vaccines.

Regarding applicants comments about TraT versus diphtheria toxoid and motivation, Russell-Jones et al. teach that immunodominant foreign T cell epitopes derived from diphtheria toxoid *were known in the art* and that diphtheria toxoid *was already approved as a carrier for human vaccines*. One of ordinary skill in the art would have been motivated to do so because immunodominant foreign T cell epitopes derived from diphtheria toxoid were known in the art and diphtheria toxoid was already approved as a carrier for human vaccines. Regarding applicants comments, Russell-Jones et al. teach Trat T cell epitopes are **inserted** into proteins, wherein the insertion of said peptide increases the antibody response against the protein into which Trat has been inserted (see page 4, lines 24-26, page 31, lines 4-8, claim 14 and Abstract). Russell-Jones et al., page 31 discloses:
"**the T cell epitope alone may be inserted within the protein antigen**". Regarding applicants comments about reasonable expectation of success, Russell-Jones et al. teach that using recombinant DNA technology that Trat peptide can be inserted into the immunogen via **substituting** Trat peptide for a peptide contained in said molecule (see page 32 and page 31, first incomplete paragraph). In addition, Bona et al. also teach that a T cell epitope can be **substituted** into a particular region of a target molecule wherein the T cell epitope retains immunogenicity (see column 11, second paragraph and column 4). Russell-Jones et al. teach that the Trat peptide is inserted such that the protein still functions as an immunogen. Regarding applicants comments about "self proteins", Russell-Jones et al. teaches that the claimed invention can be used as a vaccine in humans (see page 33) and can be used to raise antibody responses against

such proteins as luteinizing hormone, somatostatin, inhibin, FSH (eg. ***self proteins***). Russell-Jones et al. teach that, "The at least one "immunogen" which forms part of the complex *is any molecule which it is desirable to use to raise an immune response*.". Regarding applicants comments about somatostatin, there is no evidence of record that the invention of Russell-Jones et al. lacks enablement regarding this particular embodiment. The prior art is considered enabled in the absence of evidence to the contrary. No such evidence has been provided by applicant. Regarding applicants comments about reasonable expectation of success, Bona et al. also teach that a T cell epitope can be **substituted** into a particular region of a target molecule wherein the T cell epitope retains immunogenicity and have produced such molecules.

Regarding applicants comments, Russell-Jones et al. teach that their invention encompasses vaccines for use in animals and humans (see page 33). Russell-Jones et al. teach that one such immunogen could include luteinizing hormone or somatostatin or FSH or inhibin (see page 9). Said proteins could only be of two different origins (human or nonhuman). Thus, based on the disclosure of Russell-Jones et al., one of ordinary skill in the art would at once envisage use of human self-protein as a vaccine as per page 33 of Russell-Jones. Russell-Jones et al. teach Trat T cell epitopes are inserted into proteins, wherein the insertion of said peptide increases the antibody response against the protein into which Trat has been inserted (see page 4, lines 24-26, page 31, lines 4-8, claim 14 and Abstract). Russell-Jones et al. teach that the Trat peptide is inserted such that the protein still functions as an immunogen. Russell-Jones et al. teach that the Trat modified immunogen can be used as a vaccine in a composition containing an adjuvant such as saponin (see page 8 and 13). Russell-Jones et al. teach that using recombinant DNA technology that Trat peptide can be inserted into the immunogen via substituting Trat peptide for a peptide contained in said molecule (see page 31, first incomplete paragraph and claim 14 wherein the nucleic acid of claim 14 is used to recombinantly produce said protein). Russell-Jones et al. teach that immunogens used in the aforementioned vaccines can include self proteins such as luteinizing hormone, somatostatin, inhibin, FSH (see page 9 and claim 12). Russell-Jones et al. teach that such vaccines can be used in animals and humans.

One of ordinary skill in the art would have been motivated to combine the aforementioned teachings because immunodominant foreign T cell epitopes derived from diphtheria toxoid were known in the art and diphtheria toxoid was already

approved as a carrier for human vaccines. Furthermore, in the post KSR Int'l Co. v. Teleflex Inc. universe, motivation per se is not even required in a rejection under 35 USC 103. In KSR Int'l Co. v. Teleflex Inc., 550 U.S. m, 2007 WL 1237837, at "13 (2007)

it was stated that **"if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill"**.

Regarding applicants comments about unexpected results, the TraT peptides and Diphtheria toxoid derived peptides taught by Russell-Jones et al. both stimulate T cells from random donors (aka are MHC unrestricted, see Table 3) and would therefore have the functional activities referred to in page 9 of the specification. In addition, the MPEP section 716.02(d) [R-2] states:

Unexpected Results Commensurate in Scope With Claimed Invention
Whether the unexpected results are the result of unexpectedly improved results or a property not taught by the prior art, the "objective evidence of
nonobviousness must be commensurate in scope with the claims which the evidence is offered to support.".
The claims encompass methods of treating humans wherein the experiments disclosed in the specification are performed in mice. Thus, the "unexpected results" are not commensurate with the scope of the claimed invention.

9. Claim 111 is rejected under 35 U.S.C. 103(a) as being unpatentable over Russell-Jones et al. (WO 92/05192) in view of Dean et al. (US Patent 5,716,596) and Bona et al. (US Patent 5,969,109) as applied to claim 102 above, and further in view of Hellman (WO 93/05810) and Le et al. (US Patent 5,698,195).

The previous rejection renders obvious the claimed invention except for use of TNFα. Hellman teaches that modulation of self proteins responsible for manifestations of a particular disease can be achieved using self-protein conjugated to a carrier which is recognized by T helper cells(see pages 5-12) and wherein the administered hybrid molecule elicits antibodies against said molecule. Le et al. teach that antibodies against TNFα are used to treat TNFα mediated diseases in humans (see abstract and column 5). It would have been prima facies obvious to one of ordinary skill in the art at the time

the invention was made to have created the claimed invention because the use of anti TNFα antibodies to treat TNFα mediated disease was known in the art, Hellman teaches that modulation of self proteins responsible for manifestations of a particular disease can be achieved by inducing antibodies against said molecules using self molecules that contain T helper epitopes and Russell-Jones et al. teach methods for inducing antibodies against self proteins using Trat modified molecules.

Applicants arguments are as per addressed above.

10. Claims 103 and 105 are rejected under 35 U.S.C. 103(a) as being unpatentable over Russell-Jones et al. (WO 92/05192) in view of Dean et al. (US Patent 5,716,596) and Bona et al. (US Patent 5,969,109) as applied to claim 102 above, and further in view of Vitiello et al. (US 2003/0099634).

The previous rejection renders obvious the claimed invention except for use of the ovalbumin epitope recited in claim 105. Vitiello et al. disclose a peptide comprising said epitope wherein said epitope is a known immunogenic T cell epitope (see Example 7). It would have been prima facies obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because the previous rejection renders obvious the claimed invention using an immunogenic T cell epitope except for use of the particular peptide recited in the claim whilst Vitiello et al. disclose a peptide comprising said epitope wherein said epitope is a known immunogenic T cell epitope.

Applicants arguments are as per addressed above.

11. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is (571)272-0851. The examiner can normally be reached on Monday-Thursday 7:30-6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571

272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ron Schwadron/
Ron Schwadron, Ph.D.
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